Clinical Update

Naval Postgraduate Dental School
National Naval Medical Center
8901 Wisconsin Ave
Bethesda, Maryland 20889-5600

Vol. 29, No. 6 2007

Platelet rich plasma: An adjunct in regenerative wound healing

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Introduction

Contemporary dental surgery literature has recently been dominated by a variety of tissue engineering therapies including the utilization of promising new growth factor products such as enamel matrix derivative (EMD), recombinant bone morphogenetic proteins (rhBMP), and platelet rich plasma (PRP). Of these three therapies, PRP has received significant attention due to its ease of intraoperatory preparation and wide range of applications and therapeutic effects.

What is PRP?

According to Marx, who first reported on the applications and clinical benefits of platelet rich plasma in 1998, PRP is "a volume of autologous plasma that has a platelet concentration above baseline."[1] Depending on the system used for processing, platelet concentrations for PRP range anywhere from 160-740% above baseline.[2-4] To achieve therapeutic effects, however, a 400-500% increase in platelet concentration is typically required to reach the recommended PRP platelet count of 1 million/μl in a 5 ml volume.[4,5]

PRP is typically prepared by drawing either 20 or 60ml of blood from the patient on the day of surgery.[4,6] An 18 gauge catheter in the antecubital vein is recommended for ease of preparation. To obtain the highest possible number of platelets, blood should be drawn immediately prior to the initiation of surgery and before any infusion of intravenous fluid.[4] The blood is mixed with an anticoagulant and processed according to the manufacturer's directions.[4,6] Multiple studies recommend a dual-spin system in order to adequately concentrate and avoid damage to the harvested platelets.[2,4] Once prepared, PRP remains stable in an anticoagulated state for a period of 8 hours.[4,5] To activate the platelets within the PRP for release of growth factors and subsequent surgical applications, the product is combined with topical thrombin.[1,7,8]

How does PRP work?

Essentially, PRP may be considered as an autologous concentration of 8 growth factors. Within the platelet plug fraction of the PRP, growth factors such as platelet derived growth factor (PDGFaa, PDGFbb, PDGFab), transforming growth factor beta (TGF-β1, TGFβ2), vascular endothelial growth factor (VEGF), epithelial growth factor (EGF), and insulin-like growth factor (ILGF-1) are stored within platelet α granules.[3-5,7,9,10] The α granules begin secreting these growth factors within 10 minutes of the initiation of blood clotting and within 60 minutes, 95% of these factors are released.[4,5] The platelets then continue to synthesize and release additional growth factors over the next 7-8 days.[4,5]

When examined individually, the growth factors within PRP produce a multitude of effects. PDGF is a potent mitogenic and chemotactic factor for both fibroblasts and osteoblasts. In vivo studies have shown PDGF to stimulate bone formation and consistently enhance wound fill.[9,11] TGF stimulates the proliferation of osteoblast precursor cells, has a direct stimulatory effect on bone collagen synthesis, and also decreases bone resorption by inducing apoptosis of osteoclasts.[9] ILGF has been shown to enhance the differentiation of osteoblasts by increasing the expression of type I collagen as well as the rate of bone matrix apposition.[12,13] VEGF is a potent angiogenic cytokine that promotes endothelial cell proliferation and migration leading to increased vascular ingrowth.[4,14] Finally, EGF has demonstrated the ability to speed wound epithelialization and reduce scar formation.[4,15]

While each growth factor found within PRP has demonstrated unique individual properties, the combination and subsequent interaction of these factors may alter their performance. For example, the combination of PDGF and ILGF has produced a synergistic effect resulting in superior performance compared to PDGF alone.[7] In contrast to this finding, PDGF combined with TGF produced no additional benefit over TGF alone.[16] EGF, while shown to produce increased epithelialization in skin wounds, has demonstrated epithelial cell suppression in vitro.[15,16] Such mixed findings suggest that PRP may contain additional growth factors that have yet to be identified.

Clinical applications for PRP

Initial clinical applications for PRP focused on large bone grafts for the repair of craniofacial defects. The results of these studies suggested that PRP accelerated the rate of bone formation and produced greater trabecular bone density.[1] As such, early PRP studies focused on bone grafting procedures. Hanna found that periodontal intrabony defects treated with bovine-derived xenograft and PRP produced significant benefits in probing depth (PD) reduction and clinical attachment level (CAL) gains compared to bovine-derived xenograft alone.[9] Kassolis and Reynolds found that the combination of freeze dried bone allograft (FDBA) and PRP enhanced the rate of bone formation compared to FDBA and membrane in subantral augmentation grafts.[17] Since these early studies, a multitude of new clinical applications for PRP have been examined. Dermilap found endodontic applications for platelet rich plasma by successfully treating periapical inflammatory lesions with a combination of PRP and tricalcium phosphate.[10] Studies by Mancuso and Sammartino have demonstrated that PRP has the potential to improve healing of third molar extraction sites with decreased residual pocket depth formation and accelerated bony defect healing.[3,18] Separate studies by Huang and Cheung have shown applications for PRP in periodontal mucogingival procedures.[19,20] Finally, one study documented that dental implants placed in conjunction with PRP achieve accelerated bone to implant contact during the early stages of implant healing.[21]

Although the clinical applications for PRP are numerous and have shown promising benefits, a number of studies question the efficacy of this growth factor product. Raghoebar, for example, found no beneficial effect on wound healing or bone remodeling when PRP was added to subantral augmentation grafts.[22] Likewise,

Sanchez found that the addition of PRP to xenografts in the treatment of peri-implant defects demonstrated low regenerative potential.[23]

Conclusion

While findings are mixed with regards to the beneficial effect of PRP on surgical wound healing, PRP is currently the only autologous growth factor product with available intraoperatory preparation. As such, PRP possesses multiple clinical applications for dental surgical procedures and has the potential to enhance wound healing and regenerative outcomes.

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